What impact has mandatory folic acid fortification had on the incidence of colon cancer?

Conclusion

A limited body of evidence demonstrates that mandatory folic acid fortification has increased the incidence of colorectal cancer (CRC) in the US and Canada.

Grade: Limited

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades,click here.

Evidence Summary Overview

Mason et al, 2007 used the nationwide Surveillance, Epidemiology and End Result Registry, which collected data in the US and Canada from 1986 to 2002, to address the question. In the US the absolute rates of colorectal cancer (CRC) began to increase in 1996 and peaked in 1998. In Canada the absolute rates of CRC began to increase in 1997 and peaked in 2000. The sudden increase in CRC incidence represents a significant deviation from the time period just prior to folate fortification in the US by four to six additional cases per 100,000 individuals. It does not appear that changes in colorectal endoscopic procedures accounted for the increase in CRC incidence.

The study of Hirsch et al (2009) compared rates of hospital discharges due to CRC in Chile before (1992 to 1996) and after (2001 to 2004) mandatory folic acid fortification (220 mcg per 100g wheat flour). The results were described in two groups: 1) Adults aged 45 to 64 and 2) adults aged 65 to 70. In age group 1, the rate ratio of hospital discharges due to CRC was 2.6 (CI: 99% 2.93 to 2.58) for an overall increase of 162%. In age group 2, the rate ratio was 2.9 (CI: 99% 3.25 to 2.86). The authors conclude that mandatory folate fortification may be associated with an increased risk of colon cancer.

Evidence Summary Paragraphs

Hirsch et al, 2009 (neutral quality). This trend study compared the rates of hospital discharges owing to colon cancer in Chile before (1992 to 1996) and after (2001 to 2004) mandatory fortification with 220mcg folic acid per 100g wheat flour. Results were described for two groups: 1) 45 to 64 years and 2) 65 to 79 years old. In Group 1, the rate of hospital discharges owing to colon cancer increased by 162%. The highest rate ratio between the two periods was for colon cancer in Group 1 (rate ratio, 2.6, CI: 99% 2.93, 2.58) and in Group 2 (rate ratio, 2.9,CI: 99% 3.25, 2.86). These data provide new evidence that a folate fortification program could be associated with risk of colon cancer.

Mason et al, 2007 (neutral quality). This research hypothesis highlights a temporal association between folic acid fortification of enriched cereal grains in the US and Canada and an increase in the incidence of colorectal cancer (CRC) in these two countries. This paper presents a hypothetical foundation on which further research will be required to determine whether causality exists. In the

US the absolute rates of CRC began to increase in 1996 and peaked in 1998. In Canada the absolute rates of CRC began to increase in 1997 and peaked in 2000. The sudden increase in CRC incidence represents a statistically significant deviation from the pre-1996 to 1997 trends by four to six additional cases per 100,000 individuals.

View table in new window

Author, Year, Study Design, Class, Rating	Population/Sample Description	Measurements or Intervention	significant Outcomes
Hirsch S, Sanchez H et al, 2009 Study Design: Trend Study Class: D Rating:	Number of hospital discharges of two groups: 1) Before (1992 to 1996) 2) After (2001 to 2004) mandatory fortification policy in Chile. Data set collected by Chilean Ministry of Health and National Institute of Statistics.	Hospital discharge rates for colorectal, breast and gastric cancer and ischemic, hypertensive and cerebrovascular disease. Discharge rates were compared using Rate Ratios.	Rates of hospital discharge causes per 100,000 inhabitants: Group 1: (45 to 64 years old) rate ratio 2.6 (CI: 99%, 2.93 to 2.58); 1992=24.4; 1993=21.6; 1996=24.5; 2002=56.1; 2003=60.8; 2004=67.3 Group 2 (65 to 79 years old) rate ratio 2.9 (CI: 99% 3.25, 2.86); 1992=62.7; 1993=65.8; 1996=78.4; 2002=178.9; 2003=208.0; 2004=214.5.
Mason J, Dickstein A et al, 2007 Study Design: Trend study Class: D Rating:	Nationally representative data collected from the nationwide Surveillance, Epidemiology and End Result registry [which collects cancer incidence and survival data from population-based cancer registries covering ~26% of the US population and the Canadian Cancer Statistics (from 1986 to 2002)].	Colorectal endoscopic procedures.	In the US, absolute rates of CRC began to ↑ in 1996 and peaked in 1998. In Canada, absolute rates of CRC began to ↑ in 1997 and peaked in 2000. The sudden ↑ in CRC incidence represents a highly statistically significant deviation from pre-1996 to 1997 trends by four to six

			additional cases per 100,000 individuals. ↑ in rates remain statistically significant when data from each country were analyzed separately for men and women. Δ in colorectal endoscopic procedures do not seem to account for this ↑ in CRC incidence.

Research Design and Implementation Rating Summary
For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

Hirsch S, Sanchez H, Albala C, de la Maza MP, Barrera G, Leiva L, Bunout D. Colon cancer in Chile before and after the start of the flour fortification program with folic acid. *European Journal of Gastroenterology & Hepatology*. 2009; 21: 436-439.

Mason JB, Dickstein A, Jacques PF, Haggarty P, Selhub J, Dallal G, Rosenberg IH. A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: A hypothesis. *Cancer Epidemiol Biomarkers Prev*. 2007 Jul; 16 (7): 1,325-1,329.